

We claim:

1. A compound comprising the formula I-L-P, wherein:
I is an immunoglobulin heavy chain constant region or fragment thereof that
5 retains the ability to bind an Fc receptor;
L is a linker group or a direct bond; and
P is a peptide capable of binding an amyloidogenic protein.
2. The compound of claim 1, wherein I comprises the amino acid sequence
10 set forth in SEQ ID NO:1.
3. The compound of claim 1, wherein I comprises an amino acid sequence
having at least 80% identity with the amino acid sequence set forth in SEQ ID NO:1.
- 15 4. The compound of claim 1, wherein I is an IgG heavy chain constant
region or fragment thereof.
5. The compound of claim 1, wherein L is a direct bond.
- 20 6. The compound of claim 1, wherein L is a linker group.
7. The compound of claim 1, wherein P is a peptide capable of binding β -
amyloid.
- 25 8. The compound of claim 1, wherein P is a peptide capable of binding an
amyloidogenic protein selected from the group consisting of transthyretin (TTR), prion
protein (PrP), islet amyloid polypeptide (IAPP), atrial natriuretic factor (ANF), kappa
light chain, lambda light chain, amyloid A, procalcitonin, cystatin C, β 2 microglobulin,
ApoA-I, gelsolin, calcitonin, fibrinogen and lysozyme.
- 30 9. The compound of claim 1, wherein P comprises about 1-40 amino acids.
10. The compound of claim 1, wherein P comprises about 1-30 amino acids.
- 35 11. The compound of claim 1, wherein P comprises about 1-20 amino acids.
12. The compound of claim 1, wherein P comprises at least one non-naturally
occurring amino acid.

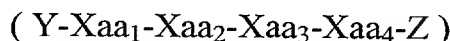
13. The compound of claim 1, wherein P comprises at least one D amino acid.

14. The compound of claim 8, wherein P comprises a subregion of an amyloidogenic protein selected from the group consisting of transthyretin (TTR), prion protein (PrP), islet amyloid polypeptide (IAPP), atrial natriuretic factor (ANF), kappa light chain, lambda light chain, amyloid A, procalcitonin, cystatin C, β 2 microglobulin, ApoA-I, gelsolin, calcitonin, fibrinogen and lysozyme.

15. The compound of claim 7, wherein P comprises a subregion of a natural β -amyloid peptide.

16. The compound of claim 7, wherein P is a peptide comprised entirely of D-amino acids and having at least three amino acid residues independently selected from the group consisting of a D-leucine structure, a D-phenylalanine structure, a D-valine structure, a D-tyrosine structure, a D-iodotyrosine structure and a D-alanine structure.

17. The compound of claim 7, wherein P is a peptide comprising the structure



wherein Xaa₁, Xaa₂, Xaa₃ and Xaa₄ are each D-amino acid structures and at least two of Xaa₁, Xaa₂, Xaa₃ and Xaa₄ are, independently, selected from the group consisting of a D-leucine structure, a D-phenylalanine structure and a D-valine structure;

Y, which may or may not be present, is a structure having the formula (Xaa)_a, wherein Xaa is any D-amino acid structure and a is an integer from 1 to 15; and

Z, which may or may not be present, is a structure having the formula (Xaa)_b, wherein Xaa is any D-amino acid structure and b is an integer from 1 to 15.

18. The compound of claim 7, wherein P is a peptide selected from the group consisting of: D-Leu-D-Val-D-Phe-D-Phe, D-Leu-D-Val-D-Phe-phenethylamide, D-Leu-D-Val-D-Tyr-D-Phe, D-Leu-D-Val-D-IodoTyr-D-Phe, D-Leu-D-Val-D-Phe-D-Tyr, D-Leu-D-Val-D-Phe-D-IodoTyr, D-Leu-D-Val-D-Phe-D-Ala, D-Leu-D-Val-D-Phe-D-Phe-D-Ala, D-Ala-D-Val-D-Phe-D-Phe-D-Leu, D-Leu-D-Val-D-Tyr-D-Phe-D-Ala, D-Leu-D-Val-D-IodoTyr-D-Phe-D-Ala, D-Leu-D-Val-D-Phe-D-Tyr-D-Ala, D-Leu-D-Val-D-Phe-D-IodoTyr-D-Ala, D-Phe-D-Phe-D-Val-D-Leu, D-Ala-D-Phe-D-Phe-D-Val, D-Ala-D-Phe-D-Phe-D-Val

D-Leu, D-Ala-D-Phe-D-Phe-D-Leu-D-Leu, D-Leu-D-Phe-D-Phe-D-Val-D-Leu, D-Phe-D-Phe-D-Phe-D-Val-D-Leu, D-Phe-D-Phe-D-Phe-D-Leu-D-Val, D-Phe-D-Phe-D-Phe-D-Phe-D-Leu, D-Ala-D-Phe-D-Phe-D-Phe-D-Leu, A β (16-30), A β (10-25), A β (1-29), A β (1-40), and A β (1-42).

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19. The compound of claim 7, wherein P is D-Leu-D-Val-D-Phe-D-Phe-D-Leu.

10 Ala.

20. The compound of claim 7, wherein P is D-Leu-D-Val-D-Phe-D-Phe-D-

21. A dimer of the compound of claim 1.

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22. A pharmaceutical composition comprising a therapeutically effective amount of the compound of claim 1 and a pharmaceutically acceptable carrier.

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23. A method for clearing an amyloidogenic protein from a subject, comprising contacting the amyloidogenic protein with the compound of claim 1 such that the amyloidogenic protein is cleared from the subject.

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24. A method for treating a subject suffering from an amyloidogenic disorder, comprising:
administering to the subject a therapeutically effective amount of the compound of claim 1, thereby treating said subject suffering from an amyloidogenic disorder.

25. The method of claim 24, wherein the amyloidogenic disorder is Alzheimer's disease.

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26. The method of claim 24, wherein the amyloidogenic disorder is a spongiform encephalopathy.

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27. A nucleic acid molecule comprising a nucleotide sequence encoding a fusion protein, said fusion protein comprising an immunoglobulin heavy chain constant region, or fragment thereof, that retains the ability to bind an Fc receptor and an amino acid sequence capable of binding to an amyloidogenic protein.

28. The nucleic acid molecule of claim 27, wherein the amyloidogenic protein is selected from the group consisting of β -amyloid, transthyretin (TTR), prion protein (PrP), islet amyloid polypeptide (IAPP), atrial natriuretic factor (ANF), kappa light chain, lambda light chain, amyloid A, procalcitonin, cystatin C, β 2 microglobulin, ApoA-I, gelsolin, calcitonin, fibrinogen, lysozyme, Huntington, and α -synuclein.

29. The nucleic acid molecule of claim 27, wherein the amyloidogenic protein is β -amyloid.

30. The nucleic acid molecule of claim 27, wherein the immunoglobulin heavy chain constant region is an IgG heavy chain constant region or fragment thereof.

31. The nucleic acid molecule of claim 30, wherein the IgG is a human, canine, bovine, porcine, murine, ovine or rat IgG.

32. The nucleic acid molecule of claim 27, wherein the immunoglobulin heavy chain constant region is an IgM, IgA, IgD or IgE heavy chain constant region or fragment thereof.

33. The nucleic acid molecule of claim 27, wherein the immunoglobulin heavy chain constant region is a human IgG heavy chain constant region or fragment thereof.

34. The nucleic acid molecule of claim 33, wherein the human IgG is IgG1, IgG2, IgG3 or IgG4.

35. The nucleic acid molecule of claim 27, wherein the immunoglobulin heavy chain constant region comprises a functionally active CH2 domain.

36. The nucleic acid molecule of claim 29, wherein the amyloidogenic protein comprises $A\beta_{1-42}$ or a fragment thereof.

37. The nucleic acid molecule of claim 36, wherein the amyloidogenic protein comprises at least four contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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38. The nucleic acid molecule of claim 36, wherein the amyloidogenic protein comprises at least five contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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39. The nucleic acid molecule of claim 36, wherein the amyloidogenic protein comprises about 4-15 contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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40. The nucleic acid molecule of claim 36, wherein the amyloidogenic protein comprises about 5-10 contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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41. The nucleic acid molecule of claim 36, wherein the amyloidogenic protein comprises a sequence selected from the group consisting of Leu-Val-Phe-Phe, Leu-Val-Phe-Phe-Ala, Leu-Val-Phe-Phe-Leu, A β (16-30), A β (10-25), A β (1-29), A β (1-40), and A β (1-42).

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42. The nucleic acid molecule of claim 36, wherein the amyloidogenic protein comprises the sequence Leu-Val-Phe-Phe-Ala (SEQ ID NO:3).

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43. The nucleic acid molecule of claim 27, wherein the fusion protein further comprises a linker group of at least one amino acid residue, said linker group linking the immunoglobulin heavy chain constant region and the amino acid sequence capable of binding to an amyloidogenic protein.

44. The nucleic acid molecule of claim 43, wherein the linker group comprises about 1-20 amino acid residues.

45. The nucleic acid molecule of claim 43, wherein the linker group comprises about 1-10 amino acid residues.

5 46. The nucleic acid molecule of claim 43, wherein the linker group comprises about 1-5 amino acid residues.

47. The nucleic acid molecule of claim 43, wherein the linker group comprises the sequence $-(\text{Gly})_n-$, wherein n is an integer of about 1-10.

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48. A vector comprising the nucleic acid molecule of any one of claims 26-47.

15 49. A recombinant cell comprising the nucleic acid molecule of any one of claims 26-47.

50. The recombinant cell of claim 49, wherein said cell is a mammalian cell.

20 51. The recombinant cell of claim 50, wherein said cell is a CHO cell or a COS cell.

52. A method of producing a polypeptide comprising culturing the recombinant cell of claim 49 in an appropriate culture medium to, thereby, produce the polypeptide.

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53. A polypeptide comprising an immunoglobulin heavy chain constant region, or fragment thereof, that retains the ability to bind an Fc receptor and an amino acid sequence capable of binding to an amyloidogenic protein.

30 54. The polypeptide of claim 53, wherein the amyloidogenic protein is selected from the group consisting of β -amyloid, transthyretin (TTR), prion protein (PrP), islet amyloid polypeptide (IAPP), atrial natriuretic factor (ANF), kappa light

chain, lambda light chain, amyloid A, procalcitonin, cystatin C, β 2 microglobulin, ApoA-I, gelsolin, calcitonin, fibrinogen, lysozyme, Huntington, and α -synuclein.

55. The polypeptide of claim 53, wherein the amyloidogenic protein is β -
5 amyloid.

56. The polypeptide of claim 53 wherein the immunoglobulin heavy chain constant region is an IgG heavy chain constant region or fragment thereof.

10 57. The polypeptide of claim 53 wherein the IgG is a human, canine, bovine, porcine, murine, ovine or rat IgG.

58. The polypeptide of claim 53, wherein the immunoglobulin heavy chain constant region is an IgM, IgA, IgD or IgE heavy chain constant region or fragment
15 thereof.

59. The polypeptide of claim 53, wherein the immunoglobulin heavy chain constant region is a human IgG heavy chain constant region or fragment thereof.

20 60. The polypeptide of claim 59, wherein the human IgG is IgG1, IgG2, IgG3 or IgG4.

61. The polypeptide of claim 53, wherein the immunoglobulin heavy chain constant region comprises a functionally active CH2 domain.
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62. The polypeptide of claim 54, wherein the amyloidogenic protein comprises $A\beta_{1-42}$ or a fragment thereof.

63. The polypeptide of claim 62, wherein the amyloidogenic protein
30 comprises at least four contiguous amino acid residues from the amino acid sequence of $A\beta_{1-42}$.

64. The polypeptide of claim 62, wherein the amyloidogenic protein comprises at least five contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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65. The polypeptide of claim 62, wherein the amyloidogenic protein comprises about 4-15 contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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66. The polypeptide of claim 62, wherein the amyloidogenic protein comprises about 5-10 contiguous amino acid residues from the amino acid sequence of A β ₁₋₄₂.

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67. The polypeptide of claim 62, wherein the amyloidogenic protein comprises a sequence selected from the group consisting of Leu-Val-Phe-Phe, Leu-Val-Phe-Phe-Ala, Leu-Val-Phe-Phe-Leu, A β (16-30), A β (10-25), A β (1-29), A β (1-40), and A β (1-42).

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68. The polypeptide of claim 62, wherein the amyloidogenic protein comprises the sequence Leu-Val-Phe-Phe-Ala (SEQ ID NO:3).

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69. The polypeptide of claim 53, wherein the fusion protein further comprises a linker group of at least one amino acid residue, said linker group linking the immunoglobulin heavy chain constant region and the amino acid sequence capable of binding to an amyloidogenic protein.

70. The polypeptide of claim 69, wherein the linker group comprises about 1-20 amino acid residues.

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71. The polypeptide of claim 69, wherein the linker group comprises about 1-10 amino acid residues.

72. The polypeptide of claim 69, wherein the linker group comprises about 1-5 amino acid residues.

73. The polypeptide of claim 69, wherein the linker group comprises the sequence $-(\text{Gly})_n-$, wherein n is an integer of about 1-10.

74. A method of preparing a therapeutic agent comprising the formula I-L-P', wherein I is an immunoglobulin heavy chain constant region or fragment thereof that retains the ability to bind an Fc receptor; L is a linker group or a direct bond; and P' is a peptide capable of binding a target protein, the method comprising:

(1) screening a peptide library to identify one or more peptides which bind to the target protein;

(2) determining the amino acid sequence of at least one peptide which binds to the target protein; and

(3) producing a therapeutic agent comprising a peptide having the amino acid sequence identified in step (2), an immunoglobulin heavy chain constant region or fragment thereof that retains the ability to bind an Fc receptor, and a linker group or a direct bond.

75. The method of claim 74, wherein the peptide library comprises L-amino acid peptides.

76. The method of claim 74, wherein the peptide library comprises D-amino acid peptides.

77. A therapeutic agent prepared by the method of claim 74.

78. A pharmaceutical composition comprising the therapeutic agent of claim 77.